(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 256 127 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication of patent specification: **16.03.94**

(51) Int. Cl.5: **C12N 9/00**, C11D 3/386, A61K 9/16, A61K 37/48

(21) Application number: **87900290.5**

(22) Date of filing: **26.12.86**

(86) International application number:
PCT/JP86/00661

International publication number:
WO 87/04184 (16.07.87 87/15)

(54) **PROCESS FOR GRANULATING ENZYME.**

(30) Priority: **27.12.85 JP 293167/85**

(43) Date of publication of application:
24.02.88 Bulletin 88/08

(45) Publication of the grant of the patent:
16.03.94 Bulletin 94/11

(84) Designated Contracting States:
DE FR GB

(56) References cited:
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JP-A- 6 028 915
JP-A-50 121 485
NL-A- 7 000 742
US-A- 3 823 090

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Description

Technical Field

This invention relates to a method for the granulation of an industrial grade raw enzyme powder. More particularly, this invention relates to a method for the granulation of a raw enzyme powder, characterized by the fact that spherical particles having diameters in a desired range can be obtained in a high yield with minimum inactivation ratio and without entailing any mechanical trouble and the produced granules possess proper strength, produce almost no dust, excel in storage, and dissolve quickly in water preparatory to actual use.

Background Art

The industrial grade enzymes which are used in medicines, foods and drinks, textiles, leather, detergents, and various other applications are broadly divided into those obtained by extraction from animals and plants and those obtained as products of fermentation by microorganisms. Generally the enzymes of the former type are economically utilizable only to a limited extent because of limited sources of supply, whereas those of the latter type are extensively used because they have virtually infinite sources of supply and are producible relatively economically.

Generally the enzyme powders, no matter whether they originate in animals and plants or in microorganisms, which have been obtained by separation and purification are rarely put to use in their unaltered form. Most of these enzyme powders are granulated by themselves or in combination with an extender, a stabilizer, and other substances and put to use.

The granulated enzymes are generally in demand in particle sizes in the range of about 0.5 to 1.5 mm. Further, as in any other field, the granulated enzymes are required to be uniform in particle size, shape, and constituent makeup, rich in flowability, excellent in mechanical strength, and rigid enough to avoid sustaining cracking and chipping during storage or transportation. Besides these general requirements, the granulated enzymes must fulfill the following requirements.

It has been pointed out that enzymes, particularly proteases (proteolytic enzyme), may cause allergic reactions in some workers and users handling them when the dust of the enzyme comes in contact with the eyes, nose, and skin, for example. Therefore, as much as possible, it is necessary to prevent generation of dust during storage, transport, use etc.

Mechanical strength and dust emission are not necessarily directly related. For example, some granules are so rigid as to offer fair resistance to disintegration and yet emit a fine dust and other granules are highly disintegrable into minute particles and yet are not reduced into a fine powder. Generally, the so-called elutriation method is used in the determination of the dust-emitting property of granulated enzymes. It is held that granulated enzymes are desirable when the amount of dust emitted thereby as determined by this method is not more than 150 GU/60 g (Ton den Ouden, Tenside Detergents, 14(1977) 4, P 209-210).

In virtually all cases, the granulated enzymes are put to use as dissolved in hot water or cold water. Particularly, in the case of granulated enzymes intended for use in detergents which form a main application for the industrial grade enzymes, from the point of the overall time consumed in laundering, these granulated enzymes must be capable of being quickly dispersed and dissolved to release the enzymes in water in a span of several minutes. Even if a granulated enzyme has high mechanical strength, therefore, it cannot be used as a good product if it possesses poor solubility in water. When an enzyme product having inferior storage stability is kept in storage for a long time, this enzyme product absorbs moisture and consequently swells and deforms, undergoes disintegration and coalescence, suffers from loss of flowability and decline of activity, and sustains other forms of degeneration, to the extent of being deprived of its commercial value. The granulated enzymes, therefore, must possess sufficient solubility in water as described above and, on the other hand, absorb moisture only nominally and exhibit satisfactory moisture resistance.

Further, in the granulation of enzyme powder, there is entailed a peculiar important problem. Enzymes are generally liable to be inactivated by heat and water. In numerous cases, their inherent activity is impaired by the heat and water to which the enzymes are exposed during the course of granulation.

Therefore, it is important for granulation method of an enzyme powder to attain the granulation under conditions not capable of inactivating the enzyme, i.e. under conditions using a low temperature and a small amount of water sufficient to preclude the inactivation of enzyme.

Quite naturally, further, the operational conditions involved in the work of granulation such as, for example, length of the time required for the granulation, presence or absence of such mechanical troubles

as adhesion of the raw material to the wall of the granulating machine, amount of such adjuvants as a binder to be used, and yield of the granulation (yield of acceptable product), viz. the conditions which may well be termed as economic factors, are equally important elements to b fulfilled.

Thus, the method adopted for the granulation of the enzyme powder can hardly be called satisfactory when it fails to fulfill all at once the numerous requirements mentioned above which, in a sense, turn out to be mutually incompatible requirements.

Various methods have been heretofore proposed as means for the granulation of enzyme powders. Substantially all of these methods, however, contemplate using water or an aqueous solution of a binder substance as the binder for the granules to be produced. Industrial grade enzymes, particularly those various enzymes which are obtained by the culture of microorganisms, generally contain impurities to a certain extent. These impurities manifest strong viscosity in the presence of water. When water is added to the raw material being granulated, therefore, it manifests its function as a binder. Since the binding force (binder property) of these impurities is variable with their composition, it is difficult to attain effective granulation of the enzyme powder under a fixed set of conditions, making it necessary to study the conditions for the granulation for each production lot of the enzyme powder. When the work of granulation is to be carried out in an automated operation, therefore, quality control of the product of this operation is difficult to obtain because the granulated enzyme acquires dispersed properties. A still more important problem arises from the fact that when an enzyme powder is granulated in the presence of water, the produced granules must be dried as by heating for expulsion of the water inevitably incorporated therein. Most enzymes by nature are relatively unstable and are liable to be inactivated in the presence of water. Thus, the presence of water itself can pose a problem. The subsequent exposure of the produced granules to the heat applied thereto for the purpose of drying aggravates the inactivation of an enzyme which inherently is rather unstable with respect to heat. Thus, the enzymatic activity is inevitably lost more or less during the course of the granulation.

Methods have been proposed for granulating enzyme powders in a non-aqueous medium using a waxy substance as a binder without the presence of water. The methods heretofore known to the art have a disadvantage that they require use of a third substance such as a core substance or fibrous substance during the work of granulation and necessitate provision of a complicated apparatus.

The method of Japanese Patent Publication SHO 46(1971)-4259, for example, effects the granulation of an enzyme powder by tumbling the raw material while using a viscous waxy substance such as a nonionic surfactant. Since this method requires to use a core substance, it produces granules with an insufficient enzyme content and further suffers from poor productivity.

Japanese Patent Publication SHO 52-47033 discloses a method which effects the granulation of an enzyme by preparing a liquid containing the enzyme and a wax as a binder, dispersing this liquid with centrifugal force, and cooling the dispersed drops of the liquid. This method does not permit a desired increase in the enzyme concentration in the produced granules because it requires use of the wax in an amount of at least 50% by weight based on the total amount of the materials for the granulation. It suffers from poor economy because the apparatus used therefor is voluminous and complicated.

Japanese Patent Publication SHO 58(1983)-26315 discloses a method for the granulation of an enzyme, which requires to use cellulosic fibers in an amount in the range of 2 to 40% by weight and a waxy substance and/or water as a granulating agent in an amount in the range of 50 to 70% by weight. This publication discloses the granulation of alkalase by the use of a water-insoluble ethoxy aliphatic alcohol, as a working example using a waxy substance as a sole granulating agent. For this method, use of cellulosic fibers having an average length in the range of 50 to 160 µ and an average width in the range of 20 to 30 µ is an essential requirement. The addition of these cellulosic fibers is claimed to preclude deposition of an irremovable layer on the inner wall of the granulating machine and facilitate the control of the granulation. From the practical point of view, however, this method has a disadvantage in that the presence of such fibers requires the waxy substance to be used in a relatively large amount, elongates the time to be spent for the granulation; and aggravates the surface irregularity of produced granules and consequently enhances the generation of dust due to friction of granules.

US-A-3 823 090 discloses a method of producing a powder detergent composition comprising mixing protease with polyethylene glycol having a molecular weight of 6,000 to form a fluid mixture, cooling said fluid mixture to form coated solid particles of protease, and mixing the thus coated particles with a detergent base containing an anionic surface active agent. The anionic surface active agents may be one or more selected among sodium, potassium and ammonium salts of fatty acids, alkylaryl sulfonates, alkylsulfates, alkylsulfonates and alkylethoxyalkylated ether sulfates. This method has the disadvantage that only solid particles having protease dispersed in polyethylene glycol which are not overcoated by a protecting coat are obtained.

In the granulation of an enzyme powder, efficiency of the work of granulation, shape and flowability of the produced granules, uniformity in the particle size, shape, and constituent makeup of the produced granules, generation of dust, rigidity, storage stability, solubility of the granules in water preparatory to actual use, and avoidance of the adverse effects exerted on the enzymatic properties by such additives as a binder are equally important considerations besides the problem of loss of activity during the course of granulation. Needless to say, economy constitutes another equally important consideration. The methods heretofore known to the art indeed possess some superior properties and exhibit improved qualities to some extent as described above. None of the conventional methods, however, can fulfill all the aforementioned considerations at once. All of them have some fault or other of their own.

Disclosure of Invention

An object of this invention is to provide a method for the granulation of a raw enzyme powder, characterized by the fact that, in the granulation of the enzyme powder alone or of a powder consisting of the enzyme and such additives as extender, stabilizer, and coloring agent (hereinafter referred to as "raw enzyme powder"), spherical particles having a particle size in a desired range can be produced in a high yield without entailing any mechanical trouble and with the inactivation during the granulation repressed to e fullest possible extent and the produced granules possess sufficient strength, excel in storage stability, produce almost no dust, and dissolve quickly in water preparatory to actual use.

The inventors continued a diligent study in search of a method for the granulation of an enzyme powder, which is capable of attaining the object described above. As a result, they have found that the granulation of an enzyme powder effected by agitating the enzyme powder in a non-aqueous system using a specific wax in an amount falling within a limited range enables uniform and substantially spherical particles to be produced quickly in a high yield without either requiring addition of a fibrous substance or entailing deposition of an irremovable layer on the inner wall of the apparatus during the course of granulation and that the produced granules possess satisfactory strength, excel in storage stability, produce almost no dust, and dissolve quickly in water preparatory to actual use. This invention has been perfected as the result.

To be specific, the present invention is directed to a method for the granulation of a raw enzyme powder, comprising the steps of:

adding to a raw enzyme powder in a substantially dry state at least one wax selected from the group consisting of (1) polyethylene glycol having a melting point in the range of 40-100 °C and an average molecular weight in the range of 3,000-10,000 and (2) polyoxyethylene-polyoxypropylene block copolymers having a melting point in the range of 40-100 °C and an average molecular weight in the range of 7,000-24,000, in an amount in the range of 10-35% by weight based on the amount of said raw enzyme powder to obtain a mixture;

agitating said mixture at a temperature 5-20 °C higher than the melting point of said at least one wax to obtain a granular material;

cooling said granulated material;

which method is characterized in that

at least one molten binder selected from the group consisting of (i) polyethylene glycol having a melting point of not less than 35 °C and not higher than the softening point of said wax and (ii) polyoxyethylene-polyoxypropylene block copolymer having a melting point of not less than 35 °C and not higher than said softening point of said wax is added to said cooled granular material, while tumbling said cooled granular material, thereby overcoating the granules of said material with said at least one binder.

Now, the method of the present invention will be described more specifically below.

The enzyme to be granulated by the method of the present invention is not specifically limited. It can be any of the enzymes which are generally used in medicines, foodstuffs, textiles, leather, detergents, and other industrial applications. The method for the granulation contemplated by this invention optimally suits enzymes to be used in detergents. The optimum enzymes for the purpose of this invention are represented by proteases, lipases, amylases, cellulases, and pectinases. One member or a combination of two or more members selected from among these optimum enzymes can be used.

The raw enzyme powder may solely comprise an enzyme powder. Otherwise, it may comprise an additive such as an extender or a filler optionally incorporated as a diluent for the purpose of keeping the specific activity of the produced granules at a prescribed level.

When the raw enzyme powder contains the aforementioned additive, the enzyme content in the raw enzyme powder is required to be at least 5% for the purpose of enabling the enzyme to be homogeneously contained in the produced granules and allowing the produced granules to retain the enzymatic activity

Comparative Experiment 9

Granules were produced by following the procedure of Example 1, except that 1,420 g of anhydrous sodium sulfate and 160 g of PEG-5000 were used instead and the time for granulation was increased to 120 minutes. No acceptable granules could be produced.

As to the particle size distribution of the produced granules, all the granules passed a 42-mesh sieve.

The same operation of granulation was repeated using PEG-species having different molecular weights of 3,000 to 10,000. No granules were obtained in any of the test runs.

Comparative Experiment 10

Granules were produced by following the procedure of Example 1, except that 820 g of anhydrous sodium sulfate and 760 g of PEG-5000 were used instead.

Two minutes after the temperature of the raw enzyme powder in the granulating machine had reached 59 °C, the molten material suddenly formed granules and this formation of granules could not easily be controlled.

The ratio of recovery was 90% and deposition of material on the inner wall of the machine was observed. The particle size distribution consisted of 70.7% of 14-mesh on, 29.1% of 14-42 mesh, and 0.2% of 42-mesh pass. Thus, the particle sizes were notably concentrated on the 14-mesh on.

The operation mentioned above was repeated using PEG-species having different molecular weights of 3,000 to 10,000 and fixing the amounts of addition at 38%. The granulation which proceeded could not be controlled in any of the test runs.

Industrial Applicability

By the method for granulation of enzyme powder according to this invention, the following effects can be obtained.

1) Since it is a specific wax that manifests the binding force required, the conditions of granulation are stable and need not be varied by the attributes of the raw enzyme powder to be used. Thus, the product of granulation acquires properties with little variance.

2) Since no water is added, the inactivation of enzyme is very slight and the enzyme activity and the yield of granulation are high.

3) Since the granulation can be carried out under substantially the same set of conditions even when the attributes of the raw material powder are varied, the productivity of the granulation by the method of the present invention is notably high.

4) In the granulation in an aqueous system, when the binder property originating in the raw enzyme powder is manifested to an excessive extent, the deposition of material to the inner wall of the granulating machine occurs heavily and the number of times of cleaning of the granulating machine is consequently high. By the method of the present invention, the deposition of material can be substantially eliminated without requiring addition of fibers.

5) The amount of a wax to be used is small, the time to be spent for granulation is shortened to half, and the yield of granulation is high as compared with the conventional granulation using fibers. The granules produced are uniform in shape and have a smooth surface. Thus, they enjoy a good appearance and yield to the phenomenon of dust emission due to friction of granules to an extremely limited extent.

6) The produced granules have low hygroscopicity, exhibit satisfactory storage stability, and excel in solubility in water. The granulated product, therefore, manifests its effect as soon as it is put to use.

7) When two or more species of enzymes, such as protease and amylase, are used in a mixed state, they do not interact within the produced granules while the granules are kept in storage, unlike the granules produced in an aqueous system. Thus, the granules have no possibility of being inactivated during the storage.

The method of this invention for the granulation of an enzyme powder will find extensive utility in medicines, foods and drinks, textiles, leather, detergents and numerous other applications.

Claims

1. A method for the granulation of a raw enzyme powder, comprising the steps of:

adding to a raw enzyme powder in a substantially dry state at least one wax selected from the group consisting of (1) polyethylene glycol having a melting point in the range of 40-100 °C and an

average molecular weight in the range of 3,000-10,000 and (2) polyoxyethylene-polyoxypropylene block copolymers having a melting point in the range of 40-100 °C and an average molecular weight in the range of 7,000-24,000, in an amount in the range of 10-35% by weight based on the amount of said raw enzyme powder to obtain a mixture;

agitating said mixture at a temperature 5-20 °C higher than the melting point of said at least one wax to obtain a granular material;

cooling said granulated material;

which method is characterized in that

at least one molten binder selected from the group consisting of (i) polyethylene glycol having a melting point of not less than 35 °C and not higher than the softening point of said wax and (ii) polyoxyethylene-polyoxypropylene block copolymer having a melting point of not less than 35 °C and not higher than said softening point of said wax is added to said cooled granular material, while tumbling said cooled granular material, thereby overcoating the granules of said material with said at least one binder.

2. The method according to claim 1, wherein the amount of said at least one binder added to the cooled granules is 6-8% by weight based on the amount of said cooled granules.

3. The method according to claim 1 or 2, wherein said polyethylene glycol wax has a melting point in the range of 45-70 °C and an average molecular weight ranging from 4,000 to 8,000.

4. The method according to any of the claims 1 to 3, wherein said polyoxyethylene-polyoxypropylene block copolymer has an average molecular weight ranging from 8,000 to 15,000.

5. The method according to any of the claims 1 to 4, wherein the temperature at which the mixture of raw enzyme powder and wax is agitated ranges from 7 °C to 12 °C.

Patentansprüche

1. Verfahren zum Granulieren eines Rohenzym-Pulvers, das folgende Schritte umfaßt:

Zufügen mindestens eines Wachses, das aus der Gruppe ausgewählt ist, die aus (1) Polyethylenglycol mit einem Schmelzpunkt im Bereich von 40 bis 100 °C und einem durchschnittlichen Molekulargewicht im Bereich von 3 000 bis 10 000 und (2) Polyoxyethylen-Polyoxypropylen-Blockcopolymeren mit einem Schmelzpunkt im Bereich von 40 bis 100 °C und einem durchschnittlichen Molekulargewicht im Bereich von 7 000 bis 24 000 besteht, in einer Menge im Bereich von 10 bis 35 Gew.-%, bezogen auf die Menge des Rohenzym-Pulvers, zu einem Rohenzym-Pulver in im wesentlichen trockenem Zustand, wobei ein Gemisch erhalten wird,

Bewegen des Gemisches bei einer Temperatur, die 5 bis 20 °C höher ist als der Schmelzpunkt des mindestens einen Wachses, wobei ein körniges Material gebildet wird,

Abkühlen des granulierten Materials, wobei das Verfahren dadurch gekennzeichnet ist, daß

mindestens ein geschmolzenes Bindemittel, das aus der Gruppe ausgewählt ist, die aus (i) Polyethylenglycol mit einem Schmelzpunkt von nicht weniger als 35 °C und nicht höher als der Erweichungspunkt des Wachses und (ii) Polyoxyethylen-Polyoxypropylen-Blockcopolymer mit einem Schmelzpunkt von nicht weniger als 35 °C und nicht höher als der Erweichungspunkt des Wachses besteht, zu dem gekühlten granulierten Material zugefügt wird, während das gekühlte granulierte Material in einer Taumelbewegung gehalten wird, wodurch die Körner des Materials mit dem mindestens einen Bindemittel überzogen werden.

2. Verfahren nach Anspruch 1, bei dem die Menge des mindestens einen Bindemittels, das zu dem gekühlten Granulat zugefügt wird, 6 bis 8 Gew.-%, bezogen auf die Menge des gekühlten Granulats, beträgt.

3. Verfahren nach Anspruch 1 oder 2, bei dem das Polyethylenglycol-Wachs einen Schmelzpunkt im Bereich von 45 bis 70 °C und ein durchschnittliches Molekulargewicht von 4 000 bis 8 000 hat.

4. Verfahren nach einem der Ansprüche 1 bis 3, bei dem das Polyoxyethylen-Polyoxypropylen-Blockcopolymer ein durchschnittliches Molekulargewicht im Bereich von 8 000 bis 15 000 hat.